REDUCED PLASMA TESTOSTERONE AND LH IN YOUNG MEN DURING PROGESTERONE ADMINISTRATION

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Heller, Laidlaw, Harvey & Nelson (1958) observed that administration of progesterone to male subjects for several weeks severely suppressed the testicular function and that, following withdrawal of the steroid, the function returned to normal within weeks. This observation might be explained by the antiandrogenic effect of progesterone (Jehan, Kamboj & Kar, 1970). It has, however, recently been shown that the synthetic gestagen medroxyprogesterone acetate will suppress both LH and testosterone when administered to male subjects (Gordon, Southren, Tochimoto, Olivo, Altman, Rand, & Lemberger, 1970).

The purpose of the present investigation has been to examine whether progesterone has the same effect as the synthetic compound on plasma testosterone and LH, which might explain the findings of Heller *et al.* (1958).

Four, healthy, male students, aged 26 to 30 years, participated in this study. Progesterone was administered as a 100-mg suppository five times daily, at 08.00, 12.00, 16.00 and 20.00 hours and midnight for 9 consecutive days in a study of the effect of progesterone on the plasma renin activity and aldosterone excretion, as published elsewhere (Sundsfjord, 1971). On the last day of progesterone administration, plasma samples were taken for the determination of testosterone and LH. About 6 months later, another blood sample was taken for the same analyses.

Testosterone was determined as described by Brownie, van der Molen, Nishizawa & Eik-Nes (1964), with modifications (Aakvaag & Vogt, 1969).

Plasma LH was determined by a radioimmunoassay technique (Norman & Turtur, 1970), which has been used in our laboratory for about 3 years. Antiserum was produced towards a commercial preparation of HCG (Pregnyl) and highly purified human pituitary LH for standards and radioiodination was performed. The coefficient of variation of duplicates from the routine is 12% in the low range (mean 2.3 ng/ml serum), which is the relevant variation since the present blood samples were carried out in one series.

Plasma progesterone was determined by the rapid competitive protein-binding method of Johansson (1969). The coefficient of variation of the method in our laboratory, calculated from duplicate determinations, is 7.8% for values between 5 and 15 ng/ml. Recovery of 0.5 to 5 ng progesterone added to plasma samples is $93\% \pm 13$ (S.D.).

During the period of progesterone administration, a plasma concentration of progesterone between 5.5 and 29 ng/ml was observed and the married students in the study did not report any change in potency or libido. The reduction of testosterone and LH levels was highly significant ($P < 0.005$, Text-fig. 1). The relatively long interval from the withdrawal of progesterone to the last blood samples excludes the possibility of a rebound effect of progesterone on these subjects.

It has been demonstrated (Rivarola, Camacho & Migeon, 1968; Gordon *et al.*, 1970) that administration of medroxyprogesterone acetate to male subjects resulted in a decrease in the plasma levels and production rate of testosterone and Gordon *et al.* (1970) noted that this decrease is concomitant with a fall in plasma LH and an increased metabolic clearance rate of testosterone. The same authors concluded that the effect of medroxyprogesterone acetate on testosterone metabolism in males is twofold, causing a decreased production rate, presumably through inhibition of pituitary LH, and an increased rate of removal of the steroid.

TEXT-FIG. 1. Testosterone and LH in plasma during and after progesterone administration. Closed bars represent values following a 9-day period of progesterone administration, open bars represent values 6 months thereafter.

The present investigation demonstrates that the physiological gestagen, progesterone, at a plasma level comparable to that observed in the normal luteal phase in women, resembles the synthetic gestagen in the ability to reduce plasma LH and testosterone. This effect of progesterone on plasma LH in normal men is not quite in agreement with the observations of Keller (1970), who found no change in urinary LH activity in postmenopausal women during administration of 50 mg of progesterone intramuscularly. It thus appears that the effect of progesterone on the hypothalamic-pituitary function may depend on the general endocrinological condition.

The findings of Heller *et al.* (1958) that administration of progesterone to male subjects led to azoospermia, decreased testicular size and a reduction in

the 17-ketosteroid excretion are fully explained by the present demonstration of a reduction of plasma LH and testosterone during progesterone administration.

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